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Our ref: AJP/GA

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Dr. J. Lederberg
The Rockefeller University,
1230 York Avenue,
New York,
NY 10021,
USA.

Dear Dr. Lederberg

Thank you very much indeed for your thoughtful letter of June 12th. The issue you raise in your first main paragraph about accelerating manifestations of AIDS is very much along the lines we are thinking. We are conscious that we are at an earlier stage in the epidemic and that the effect we may be seeing may be one mediated more by rate than any absolute difference. Although we picked out the effects on the Gc 1f homozygotes as one of the most striking observations, we strongly suspect that a Gc 1f heterozygote is also susceptible but perhaps not to such a high degree and our data is consistent with that interpretation.

We have looked at the possibility of a modification of the Gc phenotypes with time by looking at our cohort subjects and have shown that there is no change in the Gc phenotype over a period of time from when a person was a symptomless sero-positive through to when they had clinical AIDS. Although this does not totally exclude your hypothesis, I think it does diminish it. Furthermore, when we look at the overall prevelance of Gc 1f in our clinic population, it is clear that it very closely resembles that seen in the general population which would argue against there being an artifactually raised Gc 1f within the study population. We clearly wish to do a considerable amount on extending these observations in different cohorts and in particular in different risk groups and ethnic groups to try and clarify the significance of the association. Although the family studies that you suggest are certainly on our list, they are not particularly high on our list since we feel that this explanation is relatively unlikely.

Nevertheless, we very much appreciate your thoughtful suggestion and we too would urge upon our colleagues the need to evaluate Gc phenotypes in a variety of different studies around the world in order to clarify the significance of our preliminary observations. We would certainly very strongly argue that until confirmation of our observation has been possible in other studies, that the assessment of Gc phenotype should not move into the clinical arena.

With very many thanks and best wishes.

Yours sincerely,

Anthony J. Pinching
Senior Lecturer and Consultant Immunologist